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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,359	06/06/2006	Shirou Sawa	2006_0587A	6815

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EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
12/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,359	SAWA, SHIROU	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is a response to Applicant's request for reconsideration filed September 2, 2009.

Claims 1, 3, 4, and 6-9 are pending and are examined on the merits herein.

The following rejection is maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fu (US 5,414,011, May 9, 1995, PTO-1449 submitted May 5, 2006) in view of Ogawa (US 4,910,225, March 20, 2990, PTO-1449 submitted May 5, 2006, Cagle (US 6,440,964, August 27, 2002, of record) and Miyagi (US 6,281,224, August 28, 2001, PTO-1449 submitted May 5, 2008).

Fu teaches stable, clear ophthalmic formulations comprising a -COOH group-containing NSAID in combination with an antibiotic, a preservative, and a nonionic surfactant, all in an aqueous vehicle [see abstract]. Preferred embodiments comprise ketorolac (0.25-0.5% wt/vol.) and tobramycin (0.15-0.3% wt/vol.), as well as buffers and nonionic surfactants [columns 9 and 10, Examples 3-6]. Other suitable NSAIDs include indomethacin, flurbiprofen sodium, and suprofen [column 6, lines 9-16]. The

formulations are prepared by dissolving the solutes in water and adjusting the pH to about 6-8 [column 6, lines 63-67]. Suitable buffers include citrate [column 6, lines 48-50]. The ophthalmic formulations can be administered in the form of an eye drop [column 8, lines 24-35].

Fu does not teach bromfenac as the NSAID and does not teach inclusion of monoethanolamine or nicotinamide in the formulation.

Ogawa teaches ophthalmic compositions comprising bromfenac (a -COOH group-containing NSAID) [see abstract and column 5, Test drug]. The concentration of the active ingredient in a liquid preparation is preferably 0.01-5% [column 4, lines 40-46]. Bromfenac has a stronger anti-inflammatory effect than indomethacin [column 8, lines 1-2]. The solution is stabilized by the addition of a water-soluble polymer and by adjusting the pH [column 3, lines 12-15]. Buffer should be added to adjust the pH to about 6.0-9.0, preferably about 7.5-8.5 [column 3, lines 48-55]. A preferred water-soluble polymer is polyvinylpyrrolidone [column 3, lines 54-56]. The ophthalmic composition may also include other anti-inflammatory agents and an antimicrobial [column 4, lines 1-5].

Cagle teaches that cyclooxygenase type I and type II inhibitors such as diclofenac, flurbiprofen, ketorolac, supfrofen, bromfenac, and indomethacin are preferred NSAIDs for use in ophthalmic formulations comprising an antibiotic and a non-steroidal anti-inflammatory agent [column 7, lines 49-58].

Miyagi teaches opthalmic solutions containing the NSAID pranoprofen (which is also a cyclooxygenase inhibitor) and an organic amine [see abstract]. Excellent stability

and little irritation to the eyes can be prepared by the addition of organic amine [column 1, lines 59-63], preferably alkanolamines such as monoethanolamine [column 2, lines 3-5]. Surfactants such as polysorbate 80 can also be added [column 3, lines 11-40].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare an aqueous composition comprising tobramycin, bromfenac, and an alkanolamine. Bromfenac and other cyclooxygenase inhibitor NSAIDs are well known in the art for ophthalmic formulations. Aminoglycoside antibiotics such as tobramycin are also known for ophthalmic formulations. The use of aminoglycoside antibiotics along with NSAIDs is also known in the art. Ogawa teaches that polyvinylpyrrolidine can be used to help stabilize an ophthalmic solution, and Miyagi teaches that monoethanolamine can also be used to stabilize an ophthalmic solution and to reduce eye irritation. Thus, the prior art includes each element currently claimed, and each element in the combination would be expected to perform the same function as each did separately. Thus, the skilled artisan could have recognized that these elements could be combined and that the results would be predictable.

Response to Arguments

Applicant argues that Miyagi teaches many organic amines. This argument has been carefully considered but is not persuasive. Miyagi teaches that preferred organic amines are alkanolamines, sulfoalkyl piperazines, or sulfoalkyl alkylenediamines. A total of nine species are disclosed. Of the alkanolamines, there are only four. Thus,

Miyagi teaches a small number of organic amines. The skilled artisan could reasonably expect that any of this finite number of amines would be useful.

Applicant argues that monoethanolamine and nicotinamide are more effective stabilizers than N-methylglucamine. This argument has been carefully considered but is not persuasive. The skilled artisan would expect monoethanolamine to be effective based on the teachings of Miyagi. MPEP 716.02(c) states that evidence of unexpected and expected properties must be weighed, and that expected beneficial results are evidence of obviousness. The efficacy of monoethanolamine is expected based on the teachings of the prior art and is evidence of obviousness. MPEP 716.02(b) states that the evidence relied upon should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." In this case, Applicant has compared only three amines and has shown that one (N-methylglucamine) is slightly less effective than the other two. Solutions containing monoethanolamine and nicotinamide are "clear," while solutions containing N-methylglucamine are "slightly turbid." The specification (page 23) states "turbidity occurrence in the preparations was inhibited or reduced by adding an organic amine such as monoethanolamine and N-methylglucamine; nicotinamide." Thus, all of these are effective. The difference in efficacy does not appear to be significant, and the number of amines compared is very small. This number of amines and difference in their efficacy is too small to establish unexpected results based on the superiority of monoethanolamine or nicotinamide.

For these reasons, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623